MU-ACSH-SCHOOL OF MEDICINE DEPARTMENT OF PEDIATRICS AND CHILD HEALTH
LECTURE SERIES FOR C-I MEDICAL STUDENTS

Prepared by
Dr. Kiros W/gerima
(MD, Pediatrician)
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VACCINE PREVENTABLE

Lecture outlines

- Introductions
- Measles
- Tetanus
- Poliomyelitis
- Pertussis
- Diphtheria
- Chickenpox
- Mumps
- human papillomavirus
- *Haemophilus influenzae* type B
- Rubella

Objectives

- Develop knowledge of the etiology ,epidemiology and pathogenesis of common infectious diseases peculiar to children.

- Develop appropriate knowledge to clinical diagnosis and management of these childhood illnesses.

- Knowledge on possible risk factors of acquiring these infectious diseases and possible preventive methods, including immunizations.

Introduction

- *Recently, Sub Saharan Africa faces a spike of vaccine preventable diseases especially Measles where a total of 17 500 cases of Measles have been reported in the region as of January 2022, signifying an increase of 400% compared to cases reported in 2021 [5]. Some countries that have new cases of measles include Angola, Burundi, Cameroon, Central African Republic, Chad, Democratic Republic of the Congo, Ethiopia, Somalia, South Sudan, and Togo [6]. In the Sub-Saharan region, the current measles vaccine recommendations emphasize on routine administration of Measles-Mumps-Rubella (MMR) vaccine; two doses, administered to children, first dose at 12–15 months and the second dose at 4–6 years [7].*

- *This outbreak comes as an after effect of the COVID-19 pandemic, that has resulted in immunization gaps in most parts of the region [6]. Mass administration of Measles Vaccine to children is a National Campaign in most parts of the region, with an expected coverage of 95% as stipulated by World Health Organization. COVID-19 disruptions have resulted in huge strain on the heavy burdened health system, impairing the routine immunization programs leading to suspension of the vaccination drive, where about 23 million children missed out on all basic childhood vaccines in 2020.*

MEASLES

Measles Cases and Outbreaks

Español (Spanish) Print

Updated on **April 26, 2024.** CDC updates this page weekly on Fridays.

Measles cases in 2024

As of April 26, 2024, a total of 128 measles cases were reported by 20 jurisdictions: Arizona, California, Florida, Georgia, Illinois, Indiana, Louisiana, Maryland, Michigan, Minnesota, Missouri, New Jersey, New York City, New York State, Ohio, Pennsylvania, Vermont, Virginia, Washington, and West Virginia.

There have been 7 outbreaks (defined as 3 or more related cases) reported in 2024, and 67% of cases (86 of 128) are outbreak-associated. For comparison, 4 outbreaks were reported during 2023 and 48% of cases (28 of 58) were outbreak-associated. For more information on the ongoing outbreak in Chicago, Illinois see the Chicago Department of Public Health Measles Update .

Measles…Cotd

- Leading cause of morbidity and mortality among vaccine preventable diseases.
- Is an important public health problem in most developing countries (endemic in most countries).
- Most common in winter and spring
- The disease was described by the Persian physician Rhazes in the 10th century as “more dreaded than smallpox.”

Etiology

- Measles virus, an RNA virus in the family paramyxoviridae
- Only one serotype known
- Measles virus is rapidly inactivated by heat, light, acidic pH, ether, and trypsin.
- Virus shed in the nasopharyngeal secretions, blood and urine in prodromal period and for a 5-7days after rash appears.
- Viable for at least 34hours at room Temp.
- Rarely sub clinical.

epidemiology

- Endemic worldwide
- Epidemic in spring at 2-4 yr intervals as new groups of susceptible children are exposed was the rule in the pre-vaccine era.
- Prior to vaccine use the peak age was 5-10yr.
- Natural infection gives immunity for life in almost all infected.

Cont…

- Highest prevalence at age 9 mo. -2yr.(80% <5yr of age)
- **A prevalence of >90% immunization of infants has been shown to produce disease free zones.**
- The poor the community, the higher the occurrence of the infection at lower age

- The possibility that measles might be eradicated (**Biological Feasibility of Eradication) :**
  - Distinctive rash as a sentinel marker and ***accurate diagnostic tests available***
  - ***Humans are the sole pathogen reservoir***
  - No vector
  - Seasonal occurrence with disease-free periods
  - No transmissible latent virus
  - One serotype
  - An effective vaccine and ***effective intervention is available***

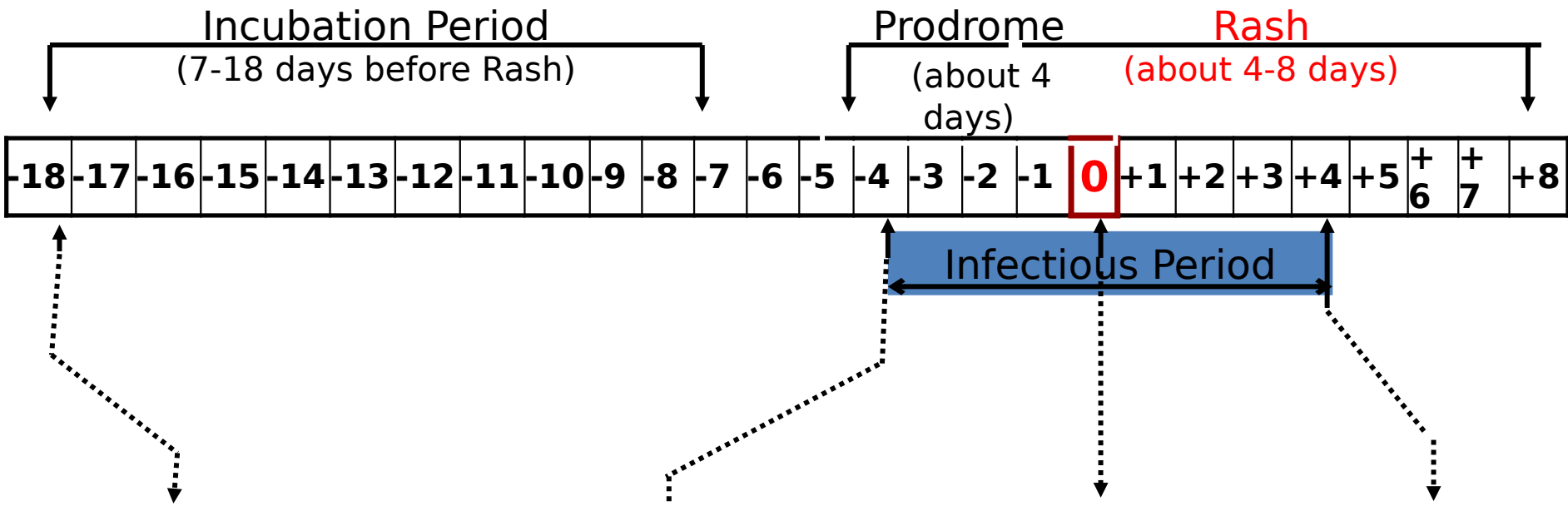
Transmission

- Portal of entry- respiratory tract or conjunctiva
- **Patients are infectious from 3-4 days before the rash up to 4–6 days after its onset**
- Nearly 90% of susceptible household contacts acquire the disease (highly contagious)
- Maximal –droplets during prodromal (cattarhal) stage
- Face-to-face contact is not necessary because viable virus may be suspended in air up to 1 hr after a source case leaves

Cont…

- Transmission occurs before diagnosis of index case
- Infants acquire passive immunity from mothers almost completely protective for 4-6 months then starts to wane at variable rates.
- Maternal antibodies undetectable usu. at 9months but may last up to 12 months (may interfere with immunization)

Clinical course of measles



Rash minus 18 days = earliest possible exposure date

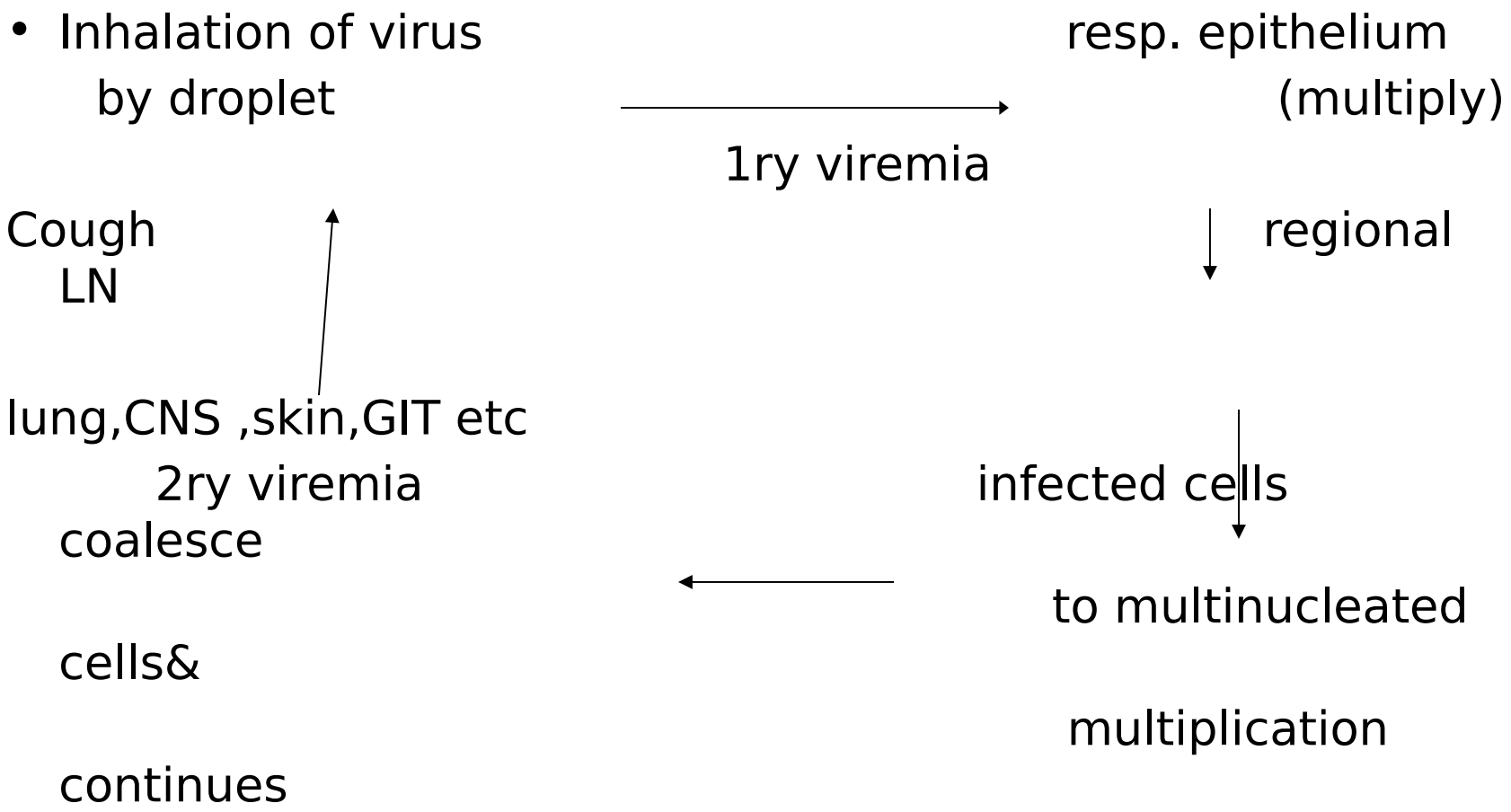
Rash minus 4 days = probable start of infectious period

Date of the onset of rash

Rash plus 4 days = probable end of infectious period

- The period when the case was exposed to measles is 7-18 days before rash onset
- It is important to find out where the case was during this period to identify all sources of exposure and possible areas of continued measles circulation

pathogenesis



Pathologic changes

skin ,mucosa & conjuctivae -serous exudates and proliferation of endothelial cells

lungs - interstitial pneumonitis (Giant cell pneumonia)

CNS - encephalitis with perivascular demyelination

IN SUBACUTE SCLEROSING PANENCEPHALITIS- degeneration of the cortex and white matter with intranuclear & intracytoplasm inclusion

Clinical features

- Three clinical stages

1) Incubating stage – lasts approximately 10-12 days to the first prodromal symptoms and another 2-4 days to the appearance of the rash

2) Prodromal stage – **lasts 3-5 days**

-low to moderate fever ,cough ,coryza and conjuctivitis followed by Koplik spots (pathognomonic sign, **a grayish white dots, usually as small as grains of sand, that have slight, reddish areolae; occasionally they are hemorrhagic , occur opposite the lower molars)**

-appears 1 to 4 days prior to the onset of the rash

Prodromal stage cont…

- **Symptoms increase in intensity for 2–4 days until the 1st day of the rash**
- A ***transverse line of conjunctival inflammation***, sharply demarcated along the eyelid margin, may be of diagnostic assistance in the prodromal stage
  - As the entire conjunctiva becomes involved, the line disappears

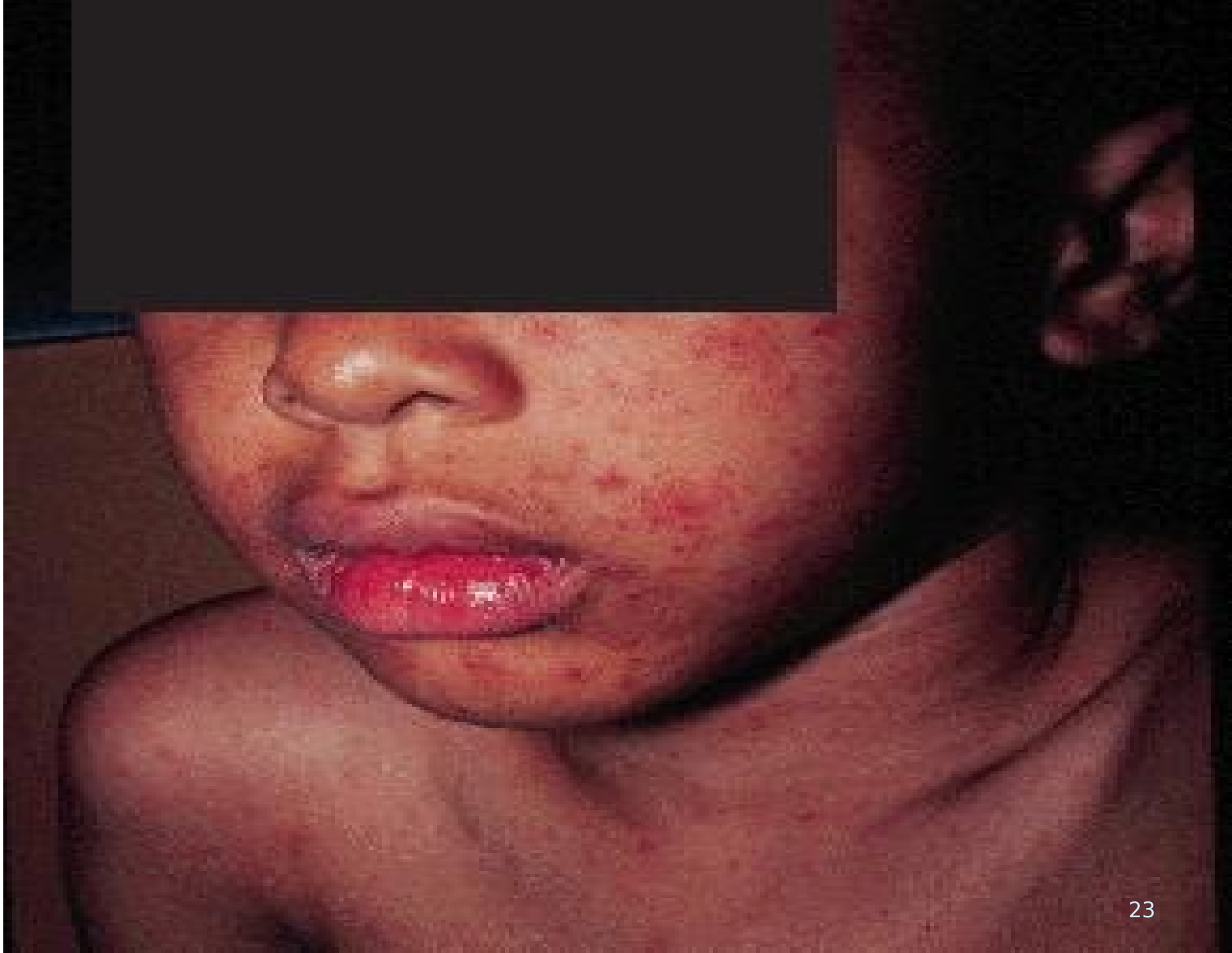
3) Erruptive stage – patient is very sick with high grade fever as rash appears & peaks for 2-3days then start to decrease.

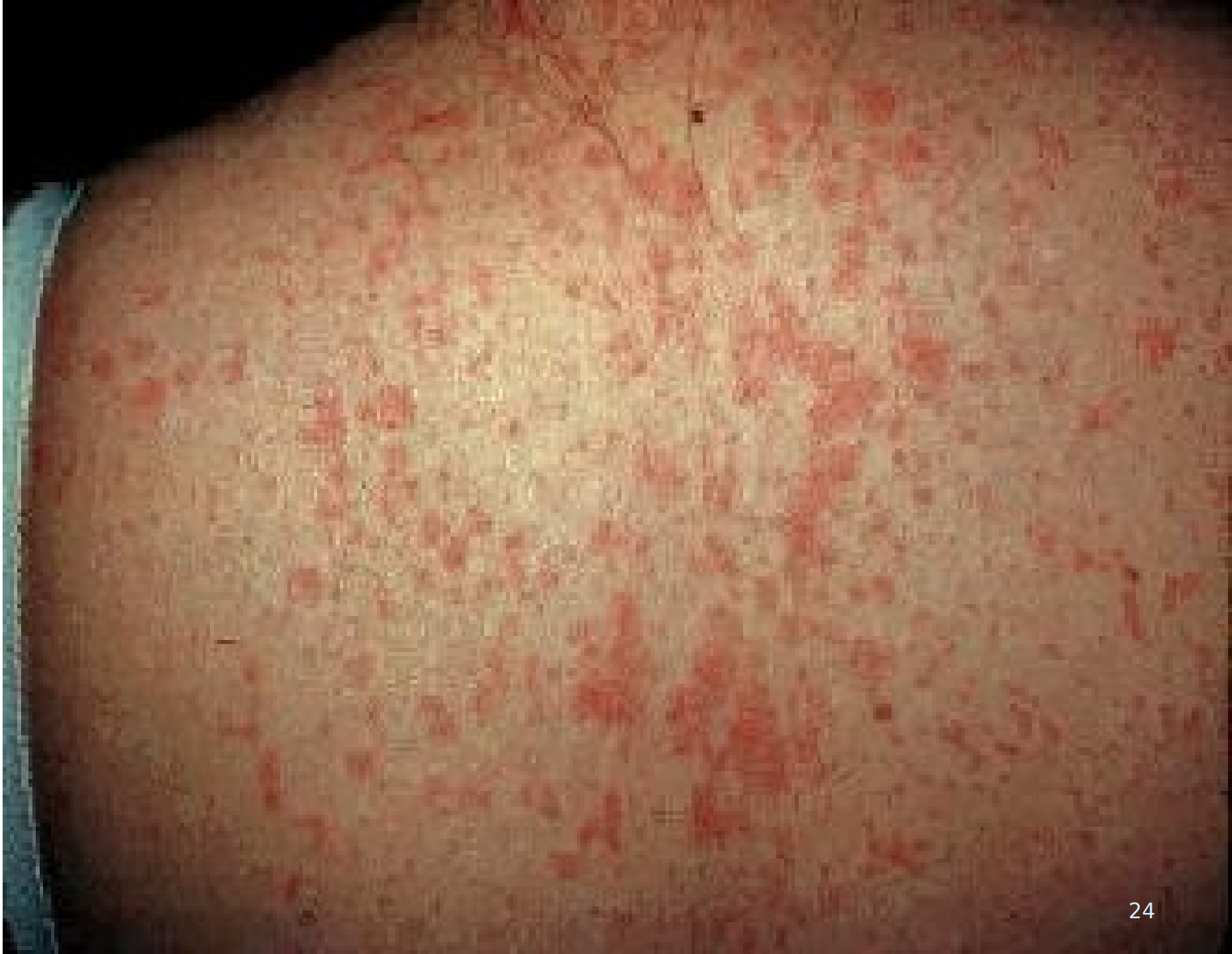
A fever which lasts >4days suggest complication

- Rash- begins around the forehead (around the hairline), behind the ears, and on the upper neck as a red maculopapular eruption, then spreads downward to the torso and extremities, reaching the palms and soles in up to 50% of cases.
  - spread centrifugally to involve the feet by 2nd to 3rd day
  - With the onset of the rash, symptoms begin to subside
  - the rash fades over about 7 days in the same progression as it evolved, often leaving a fine desquamation of skin in its wake
  - the more confluent and extensive, the more severe the disease
  - posterior cervical LAP
  - abd. Pain – suggests mesentric lymphadenitis may mimic appendicitis,slight splenomegaly
  - diarrhea, pneumonia, otitis media---common in infants and young children

.

- Black measles(hemorrhagic type)- bleeding from mouth ,nose or bowel may occur
- Atypical measles - in recipients of killed vaccine who later exposed to wild virus----no typical symptom except fever
- rash first appears on the palms, wrists, soles, and ankles, and progresses in a centripetal direction





LABORATORY FINDINGS

- white blood cell count tends to be low with a relative lymphocytosis
- Absolute neutropenia (rare)

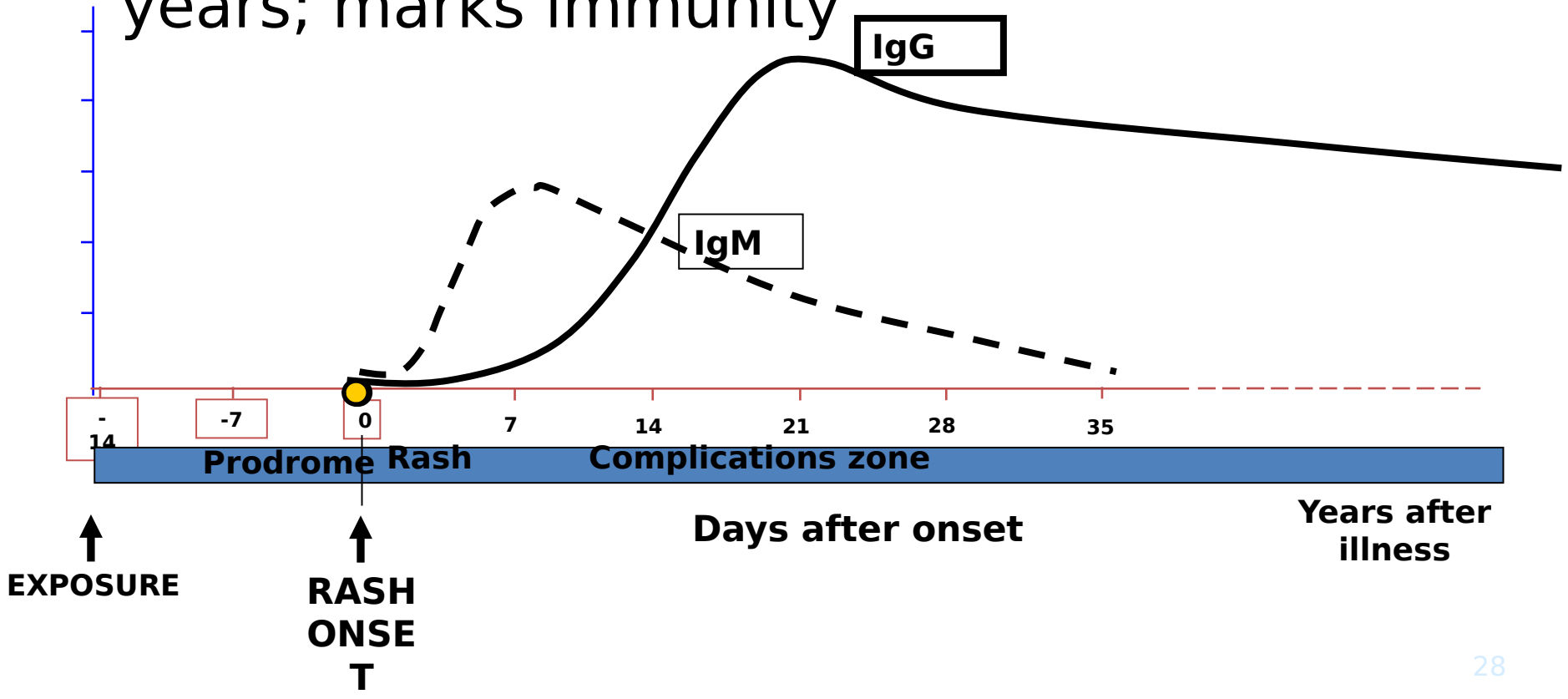
- Diagnosis
  - mainly clinical with epidemiologic findings
  - **Serologic confirmation**
    - IgM antibody appears 1–2 days after the onset of the rash and remains detectable for about 1 mo.
    - **a 4-fold rise in IgG antibodies in acute and convalescent specimens taken 2–4 wk later**
  - viral culture (**from blood, urine, or respiratory secretions)**

All suspected should be reported!!

CSF in measles encephalitis-increased ptn & small increase in lymphocytes

Measles infection and antibody response

- IgM appears first and disappears within 30 days; marks the acute infection
- IgG appears later and remains high for years; marks immunity



DDX

- **Rubella-rash appears and disappears in 24hrs**
- **Roseola infantum-** The rash appears as the fever disappears
- **Toxo, scarlet fever, coxsackie v., drug rash etc**
- **Meningococcemia**

- **Complications**
  - **Attributable to the pathogenic effects of the virus on the respiratory tract and immune system**
  - Respiratory –most common cause of death
    - Otitis media (5 -15%)
    - Pneumonia- measles interstitial pneumonitis (Giant cell pneumonia)

      (5 – 10%) by aureus and -secondary bacterial pneumonia strept. Pneumonae, staph. haemophilus inf.
    - Measles croup, laryngitis , trachitis
    - Tuberculosis reactivation is common-b/se of impaired cellular immunity for 1-2months
    - Sinusitis and mastoiditis

Cont…

- GI- AGE with viral & bacterial agents, persistent diarrhea
- Malnutrition
- Eye - corneal ulceration

  - blindness due to exacerbation of xerophthalmia &/or direct viral keratoconjuctivitis
- CNS - encephalitis with sequele such as MR & seizure in 1/3 and 1/3 die
- SUBACUTE SCLEROSING PANENCEPHLITIS - rare, causes chronic encephalitis due to persistent viral infection

  - occurs after 5-15yr of 1st infection- myoclonic seizure with progressive dementia, most die in 6-9months

- **Treatment**
  - **Supportive**
    - Antipyretics
    - bed rest
    - adequate fluid intake
    - home remedies for laryngitis & irritating cough
    - warm and dim room
  - **Treatment of complications**
    - antibiotic for bacterial infections
    - Ig & corticosteroids has no role
    - Vitamin A (hyporetinemia is present in >90% of patients)
    - nutritional support for malnutrition and diarrhea
    - Enhance infection control in hospitals
- Advise mother to:
  - Reduce fever with antipyretics
  - Bring the child back if the illness worsens
  - Give fluids and extra food

Prognosis

- Case fatality from measles :
  - 1 – 10%
  - As high as 30% in famine, refugee populaitons
- Prevention
  - Isolation precautions, especially in hospitals and other institutions, should be maintained from the 7th day after exposure until 5 days after the rash has appeared.
  - Vaccination- measles live attenuated vaccine has >95% efficacy

POSTEXPOSURE PROPHYLAXIS

- Passive immunization with immune globulin is effective for prevention and attenuation of measles within 6 days of exposure
  - Susceptible household and hospital contacts who are younger than 12 mo of age
  - Pregnant women and immunocompromised persons
  - Infants 6 mo of age or younger born to nonimmune mothers
  - Live virus vaccines should be given 3 weeks before or 3 months after the injection of the human immune globulin.
- Vaccination within 72 hrs
  - Susceptible children 6-12 mo of age
  - Susceptible children 12 mo of age or older
  - In case of epidemics, the vaccine can be given to children above the age of 6 months but this should not be counted and they should be given another dose at the proper schedule.

Measles Mortality Reduction Strategies

1. Routine immunization coverage ≥ 80%
2. Provide second opportunity for measles immunization
3. Intensified case based surveillance with lab confirmation
4. Improved case management

1. Measles routine immunisation

- Attain high coverage in routine infant measles vaccination;
  - one of the key indicators of the attainment of the MDGs

3. Case-based Surveillance

- Notification, investigation and collection of epidemiologic information and serum specimens from **all suspected cases**:
  - For serologic testing for measles IgM
  - For identification of circulating strains of measles viruses (only in outbreak settings

Measles Case Definitions

- Clinical measles = suspected case:
  - **Fever + rash + *cough* or *conjunctivitis* or *coryza***
    - or -
  - Clinician diagnosed measles

- Confirmed measles cases:
  - Lab confirmed measles:
  - Measles confirmed by epidemiological linkage

Tetanus

- Acute, spastic paralytic illness caused by the neurotoxin produced by *Clostridium tetani (*long, thin, motile, gram-positive spore-forming obligate anaerobic rod)
- Endemic in approximately 90 developing countries

Predisposing factors

- A penetrating injury resulting in the inoculation of C. tetani spores
- Burns
- Animal bites
- Circumcision, etc

PATHOGENESIS

- Introduced spores germinate, multiply, and produce tetanus toxin →Toxin is released after vegetative bacterial cell death and lysis →toxin binds at the neuromuscular junction and enters the motor nerve by endocytosis →undergoes retrograde axonal transport to the cytoplasm of the α-motoneuron →toxin exits the motoneuron in the spinal cord and next enters adjacent spinal inhibitory interneurons →prevents release of the neurotransmitters glycine γ-aminobutyric acid (GABA) →blocks the normal inhibition of antagonistic muscles on which voluntary coordinated movement depends

CLINICAL MANIFESTATIONS

- Can present in one of four clinical patterns:
  - Generalized
  - Local
  - Cephalic
  - Neonatal
- Incubation period typically is 2–14 days (may be as long as months)

Cont…

- Generalized tetanus
  - Trismus (masseter muscle spasm, or lockjaw)
  - Sardonic smile of tetanus (risus sardonicus)
  - Opisthotonos (an arched posture of extreme hyperextension of the body)
  - Laryngeal and respiratory muscle spasm →airway obstruction and asphyxiation
  - Seizures (sudden, severe tonic contractions of the muscles, with fist clenching, flexion, and adduction of the arms and hyperextension of the legs)

Cont...

- Dysuria and urinary retention (bladder sphincter spasm) and forced defecation
- Fever, as high as 40°C
- Autonomic effects:
  - Tachycardia,
  - Dysrhythmias,
  - Labile hypertension,
  - Diaphoresis, and
  - Cutaneous vasoconstriction

Toxin does not affect sensory nerves or cortical function → the patient remains conscious, in extreme pain, and in fearful anticipation of the next tetanic seizure

The tetanic paralysis usually becomes more severe in the 1st wk after onset, stabilizes in the 2nd wk, and ameliorates gradually over the ensuing 1–4 wk

Cont...

- Localized tetanus
  - Results in painful spasms of the muscles adjacent to the wound site and
  - May precede generalized tetanus

- Cephalic tetanus
  - Rare form of localized tetanus involving the bulbar musculature
  - Occurs with wounds or foreign bodies in the head, nostrils, or face
  - May occur in association with chronic otitis media.
  - Characterized by
    - Retracted eyelids,
    - Deviated gaze,
    - Trismus,
    - Risus sardonicus, and
    - Spastic paralysis of the tongue and pharyngeal musculature.

Cont...

Neonatal tetanus (tetanus neonatorum)

- Infantile form of generalized tetanus
- Manifests within 3–12 days of birth as:
  - Progressive difficulty in feeding (sucking and swallowing), associated hunger, and crying
  - Paralysis or diminished movement,
  - Stiffness and rigidity to the touch, and
  - Spasms, with or without opisthotonos

Duration of illness

- Tetanus toxin-induced effects are long-lasting because recovery requires the growth of new axonal nerve terminals
- Usual duration of clinical tetanus is 4 to 6 weeks

Diagnosis

- Usually clinically
- Typical setting - an unimmunized patient (and/or mother) who was injured or born within the preceding 2 wk, who presents with
  - Trismus,
  - Other rigid muscles, and
  - Clear sensorium
- Peripheral leukocytosis - from secondary bacterial infection or stress

Treatment

- The goals of treatment include:
  - Eradication of *C. tetani* and the wound environment conducive to its anaerobic multiplication (halting the toxin production),
  - Neutralization of unbound toxin,
  - Control of seizures/muscle spasms and respiration,
  - Management of dysautonomia
  - Palliation and provision of meticulous supportive care, and
  - Prevention of recurrences

Halting toxin production

- Surgical wound excision and debridement
- Antimicrobial therapy - - Penicillin G (100,000 U/kg/day divided every 4–6 hr IV for 10–14 days)

Neutralization of unbound toxin

- Administration of human tetanus immunoglobulin (TIG) as soon as possible (500U IM)
- If TIG is unavailable, use of human intravenous immunoglobulin (IVIG),
- Tetanus antitoxin (10,000 U half IM ,half IV)

Control of muscle spasms

- Sedatives – Diazepam and chlopromazine alternately
- Neuromuscular blocking agents - when sedation alone is inadequate

Management of autonomic dysfunction

- Magnesium sulphate/morphine
- Esmalol

Supportive care

- Main treatment for tetanus
- Supportive care in a quiet, dark, secluded setting
- Patient should be sedated and protected from all unnecessary sounds, sights, and touch
- Endotracheal intubation as necessary
- Early tracheostomy in severe cases
- Cardiorespiratory monitoring
- Maintenance of the substantial fluid, electrolyte, and caloric needs
- Nursing care to mouth, skin, bladder, and bowel function
- P

Complications

- Aspiration of secretions and pneumonia
- Pneumothorax and mediastinal emphysema
- Fracture
- Venous thrombosis
- Pulmonary embolism
- Gastric ulceration with or without hemorrhage,
- Paralytic ileus
- Decubitus ulceration
- Cardiac arrhythmias
- Unstable blood pressure
- Labile temperature regulation
- Rhabdomyolysis with myoglobinuria and renal failure

Prognosis

- The most important factor that influences outcome is the quality of supportive care
- Most fatalities occur within the 1st wk of illness
- Sequelae of hypoxic brain injury, especially in infants, include cerebral palsy, diminished mental abilities, and behavioral difficulties
- Case fatality rates:
  - Generalized tetanus - 5–35%,
  - Neonatal tetanus - from <10% with intensive care treatment to >75% without it
- Unfavorable prognosis in :
  - Incubation period $\leq$ 7 days
  - Period of onset < 3 days
  - Presence of fever
  - Extremes of age
  - Cephalic tetanus

Prevention

- Preventable disease
- A serum antibody titer of ≥0.01 U/mL is protective
- Active immunization in early infancy
- Immunization of women with tetanus toxoid
- Recovered individuals do not necessarily develop “natural Immunity” against the infection---because the very small amount of tetanus toxin produced during the infection does not elicit a strong, protective immune response which would produce enough antibodies against future re-infection

* ***All patients with tetanus should be vaccinated with TT at discharge with provision for completion of the primary series (*****Provide active immunization with appropriate booster doses in those who were never immunized in the past**)

Tetanus Prophylaxis in Routine Wound Management

	CLEAN, MINOR WOUNDS		OTHER WOUNDS	
HISTORY OF ABSORBED TETANUS TOXOID (DOSES)	**Tdap or Td**	**TIG**	**Tdap or Td**	**TIG**
Uncertain, or <3	Yes	No	Yes	Yes
3 or more	No	No	No	No

Severity grading of tetanus

Grading of severity	
Grade 1 (mild):	Mild to moderate trismus and general spasticity, little or no dysphagia, no respiratory embarrassment
Grade 2 (moderate):	Moderate trismus and general spasticity, some dysphagia and respiratory embarrassment, and fleeting spasms occur.
Grade 3a (severe):	Severe trismus and general spasticity, severe dysphagia and respiratory difficulties, and severe and prolonged spasms (both spontaneous and on stimulation).
Grade 3b (very severe):	The same as for severe tetanus plus autonomic dysfunction, particularly sympathetic overdrive.

Pertussis

- Pertussis = intense cough
- Some times called **whooping cough**
- ETIOLOGY
  - *Bordetella pertussis* – commonest
  - *Bordetella parapertussis* - occasional cause
- EPIDEMIOLOGY
  - There are 60 million cases of pertussis each year worldwide, resulting in >500,000 deaths
  - extremely contagious, with attack rates as high as 100% in susceptible individuals exposed to aerosol droplets
  - Neither natural disease nor vaccination provides complete or lifelong immunity against reinfection or disease
  - Protection against typical disease begins to wane with age (3–5 yr after vaccination and is unmeasurable after 12 yr)

PATHOGENESIS

- *B. pertussis* expresses ***Pertussis toxin (PT),*** the major virulence protein:
  - Promotes attachment to respiratory epithelium
  - Sensitizes to histamine
  - Elicits lymphocytosis
  - Enhances insulin secretion
  - Causes T-lymphocyte mitogenesis
  - Stimulates production of interleukin-4 and immunoglobulin E
  - Inhibits phagocytic function of leukocytes
- *B. pertussis* also produces other biologically active substances
  - filamentous hemagglutinin (FHA) – for attachment
  - Agglutinogens (fimbrae) – e.g pertactin which is important for attachment
  - Tracheal cytotoxin - inhibit clearance of organisms, responsible for the local epithelial damage that produces respiratory symptoms and facilitates absorption of PT

CLINICAL MANIFESTATIONS

- pertussis is a prolonged disease divided into:
  - catarrhal - 1–2 wk
    - nondistinctive symptoms of congestion and rhinorrhea variably accompanied by low-grade fever, sneezing, lacrimation, and conjunctival suffusion
  - paroxysmal - 2–6 wk
    - a dry, intermittent, irritative cough evolving into the inexorable paroxysms that are the hallmark of pertussis
    - loud whoop follows as inspired air traverses the still partially closed airway
    - Post-tussive emesis is common
  - convalescent stages (≥2 wk),
    - The number, severity, and duration of episodes diminish
  - Infants <3 mo of age may have apnea, cyanosis, or an acute life-threatening event

DIAGNOSIS

- Mainly clinical when patient has classical manifestations
- Leukocytosis (15,000–100,000 cells/mm^3) due to absolute lymphocytosis is characteristic in the catarrhal stage
- Chest x-ray - may show perihilar infiltrate or edema (sometimes with a butterfly appearance) and variable atelectasis
- Isolation of *B. pertussis* in culture remains the gold standard for diagnosis
  - Regan-Lowe charcoal agar
  - Stainer-Scholte media
- **Clinical case definition -** cough of ≥14 days' duration with at least 1 associated symptom of paroxysms, whoop, or post-tussive vomiting

TREATMENT

- Goals of therapy are to:
  - Limit the number of paroxysms,
  - Observe the severity of the cough,
  - Provide assistance when necessary, and
  - Maximize nutrition, rest, and recovery without sequelae
- Admission:
  - All infants below 6 months
  - If significant complications occurred
  - Children with underlying cardiac, pulmonary, muscular, or neurologic disorders

Rx cont…

- Supportive
  - Small frequent feeding
  - IV fluids if very frequent vomiting
  - O_2 if in distress
  - Monitor for apnea in infants
- Antibiotics
    - Erythromycin to break transmission and as a prophylaxis for all household members and other contacts
    - Start as early s possible
- Isolation - respiratory isolation

Complication

- Infants <6 mo of age have excessive mortality and morbidity
- ***Respiratory*** - Pneumonia (commonest), atelectasis, pneumothorax, emphysema, bronchiectasis, otitis media
- ***Malnutrition***
- ***CNS*** – Seizure, encephalopathy, intracranial hemorrhage
- ***Physical sequele*** – hernias, rectal prolapse, hemorrhage (Conjunctival, scleral and retinal hemorrhages, petechiae on the upper body, epistaxis)

PREVENTION

- Universal immunization of children with pertussis vaccine, beginning in infancy with periodic reinforcing doses
- Vaccines – DTaP / DTP
- In our country – DTP used
- Given at the age of 6wks, 10wks & 14wks
- Adverse effects – rare
  - high fever, persistent crying of ≥3 hr duration, hypotonic hyporesponsive episodes, and seizures
  - May require exemption of subsequent vaccination

Diphtheria

- **From the Greek word for leather which refers to the tough pharyngeal membrane that is the clinical hallmark of infection**
- **Acute toxic infection caused by *Corynebacterium* species, typically *Corynebacterium diphtheriae***
- ***Corynebacterium ulcerans –rarely***
- **aerobic, nonencapsulated, non-spore-forming, mostly nonmotile, pleomorphic, gram-positive bacilli**
- **exclusive inhabitant of human mucous membranes and skin**
- CDC describes diphtheria as "an upper respiratory tract illness characterized by sore throat, low-grade fever, and an adherent membrane of the tonsil(s), pharynx, and/or nose".

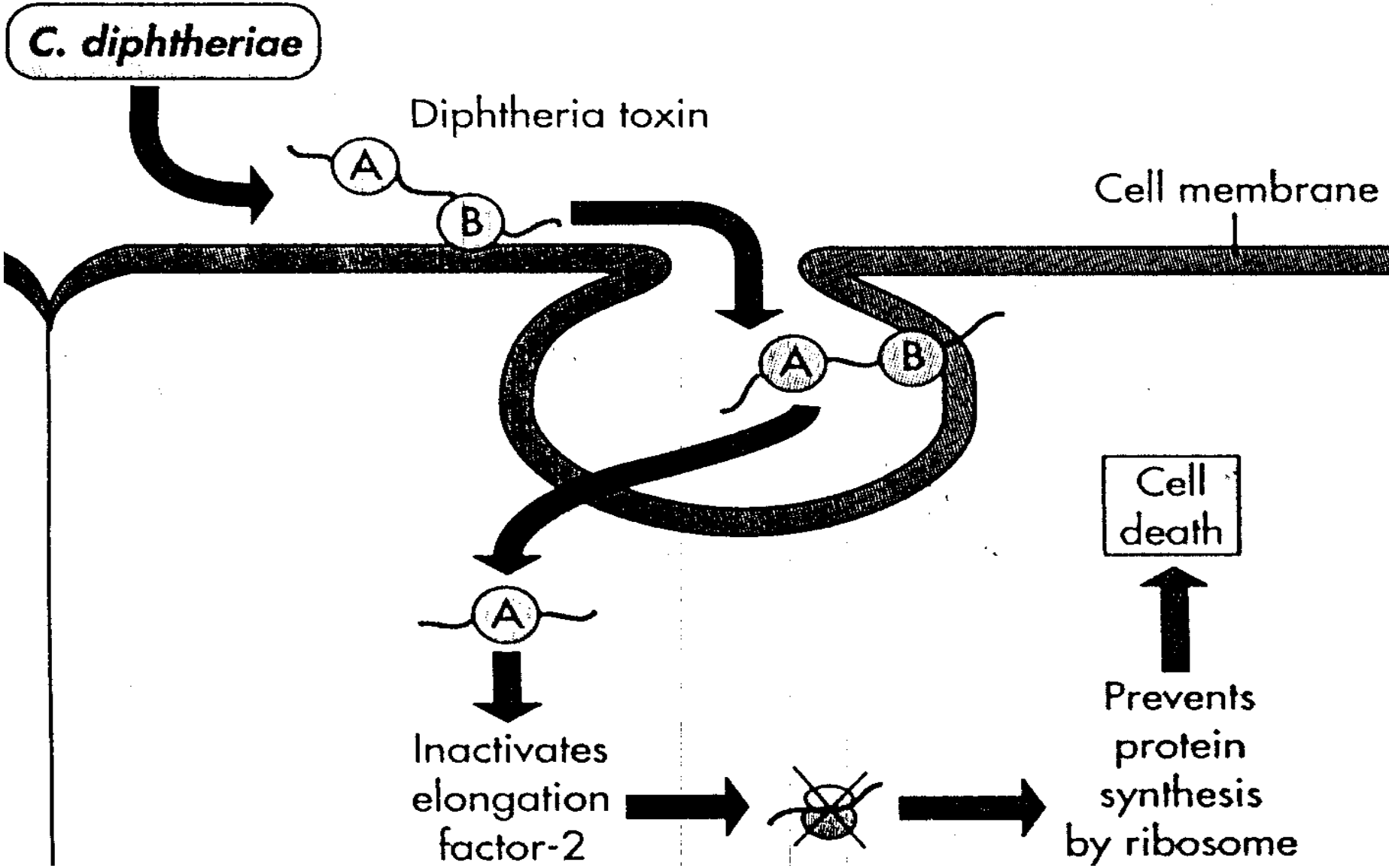
Transmission

- Person to person contact by:
  - airborne respiratory droplets (inhalation),
  - direct contact with respiratory secretions of symptomatic individuals, or exudate from infected skin lesions
  - Asymptomatic carriage maintains bacteria in population -important in transmission
- Organisms can remain viable in dust or on fomites for up to 6 mo
- Transmission through contaminated milk and an infected food handler has been proved or suspected.

PATHOGENESIS

- Both toxigenic and nontoxigenic *C. diphtheriae* cause skin and mucosal infection
- usually remains in the superficial layers of skin lesions or respiratory tract mucosa, inducing local inflammatory reaction
- major virulence of the organism- exotoxin, which inhibits protein synthesis and causes local tissue necrosis
- A dense necrotic coagulum of organisms, epithelial cells, fibrin, leukocytes, and erythrocytes forms, advances, and becomes a gray-brown, leather-like adherent - Pseudomembrane

Mechanism of Action of Diphtheria Toxin:



Pathogenicity

- **two distinct phenomena**:
  - **Invasion** of the local tissues of the throat, which requires colonization and subsequent bacterial proliferation
  - **Toxigenesis**: bacterial production of the toxin
- Two factors have great influence on the ability of *Corynebacterium diphtheriae* to produce the diphtheria toxin:
  - **low extracellular concentrations of iron**
  - the **presence of a lysogenic prophage (virus)** in the bacterial chromosome

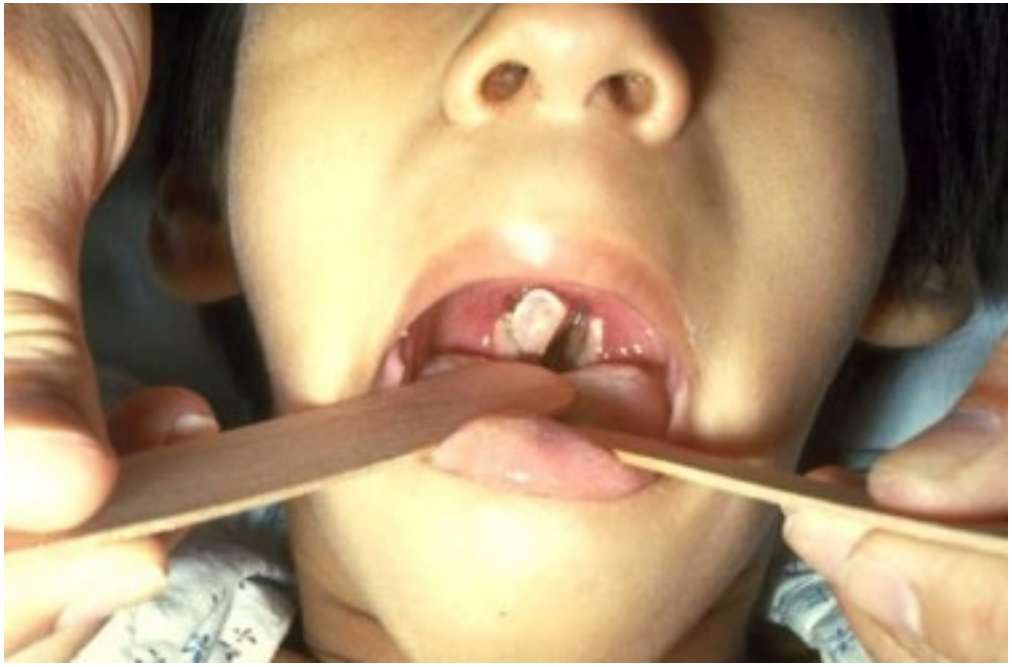
CLINICAL MANIFESTATIONS

- **Influenced by the**
  - **Anatomic site of infection,**
  - **The immune status of the host, and**
  - **The production and systemic distribution of toxin**
- Classified based on site of infection
  - **Anterior nasal**
  - **Pharyngeal and tonsillar**
  - **Laryngeal**
  - **Cutaneous**
  - **Ocular**
  - **Genital**

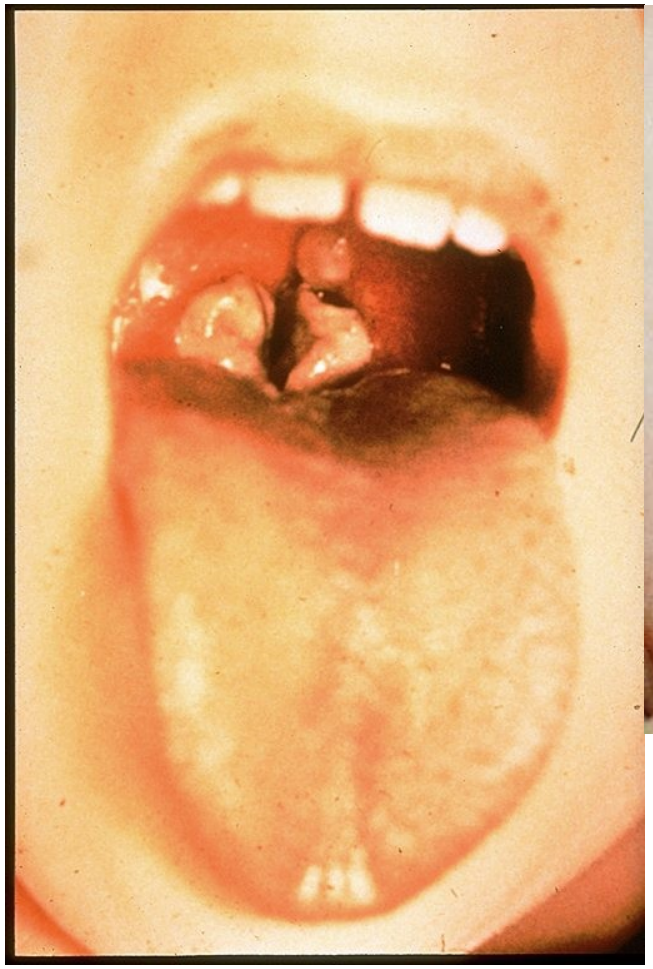
Respiratory Tract Diphtheria

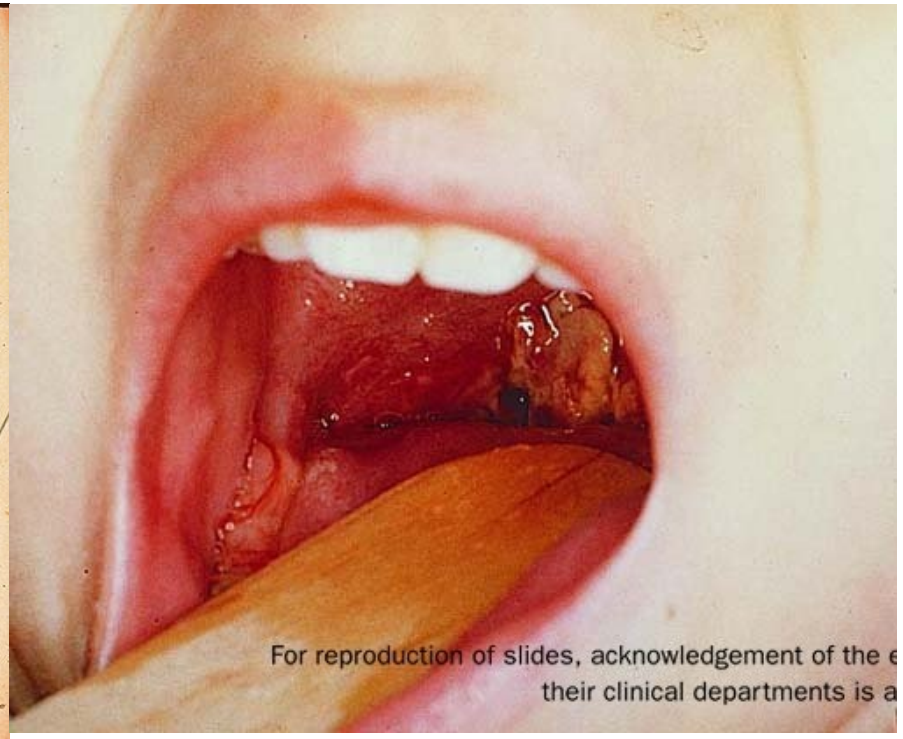
- **Incubation period of 2–4 days**
- May involve any mucous membrane
- **Infection of the anterior nares,**
  - **serosanguineous, purulent, erosive rhinitis with membrane formation**
  - **Shallow ulceration of the external nares and upper lip**
- **In tonsillar and pharyngeal diphtheria,**
  - **Sore throat**
  - **Dysphagia, hoarseness, malaise, or headache**
  - **Exudate spreads within 2-3 days and may form adherent pseudo membrane**
  - **Membrane may cause respiratory obstruction**
  - **Fever (Only half of patients) usually not high but patient appears toxic**

Thick Membrane

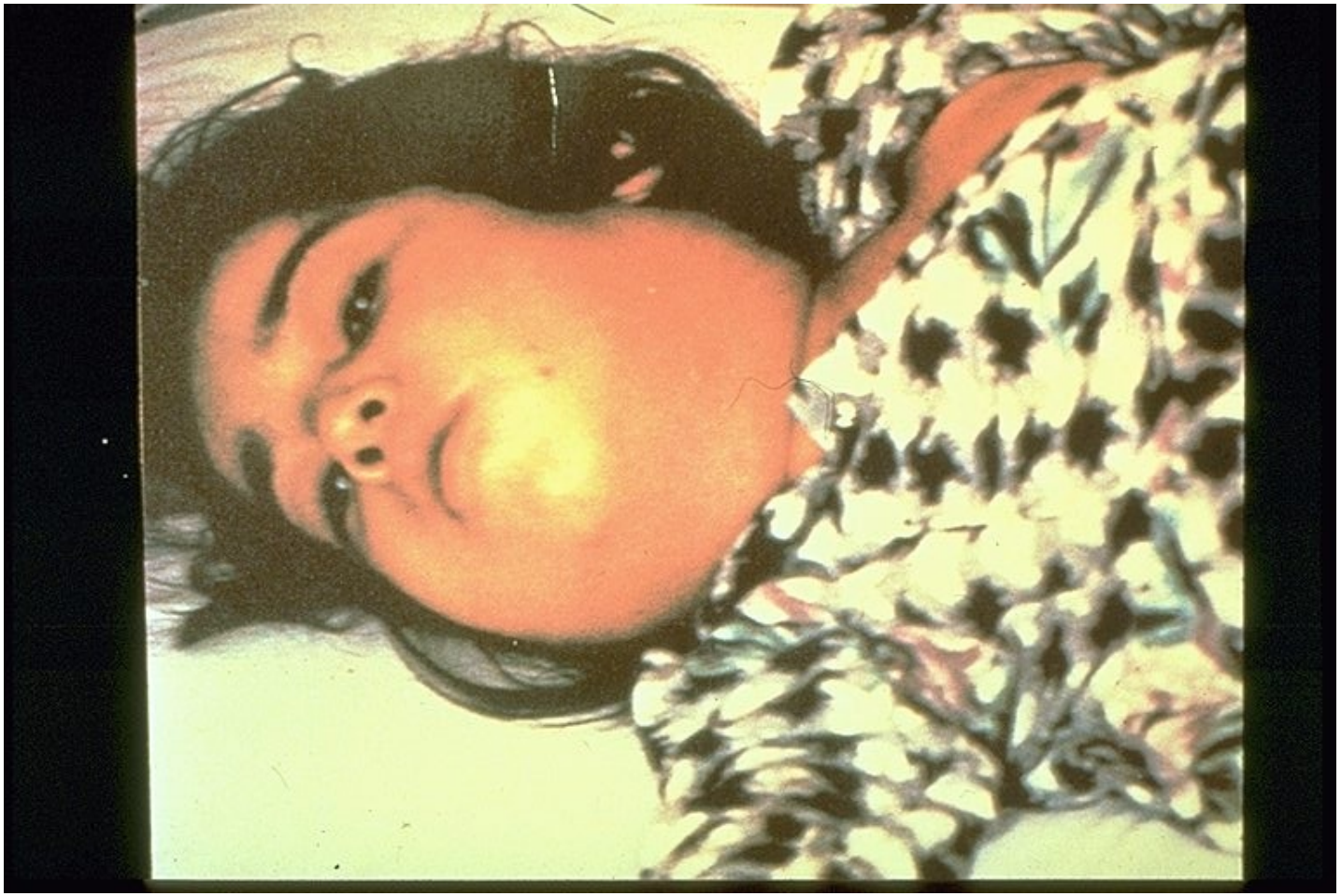


Pseudo membrane





‘Bull Neck’



Cont...

- **Mild pharyngeal injection is followed by unilateral or bilateral tonsillar membrane formation**
- **Underlying soft tissue edema and enlarged lymph nodes can cause a bull-neck appearance**
- **The degree of local extension correlates directly with profound prostration, bull-neck appearance, and fatality due to airway compromise or toxin-mediated complications**

Cont…

- **laryngeal diphtheria**
  - **significant risk for suffocation because of local soft tissue edema and airway obstruction by the diphtheritic membrane, a dense cast of respiratory epithelium, and necrotic coagulum**
  - **Establishment of an artificial airway and resection of the pseudomembrane is lifesaving**
  - **further obstructive complications are common, and systemic toxic complications are inevitable**

Cont…

- The diphtheritic membrane is tightly adherent to underlying tissue (resulting in bleeding with dislodgement), is sharply demarcated, and is classically gray in color
- The *infectious period*, in untreated patients, begins at symptom onset and continues for two weeks in the majority of patients and as long as six weeks in some patients
- communicability usually lasts less than four days if the patient is treated with appropriate antibiotics

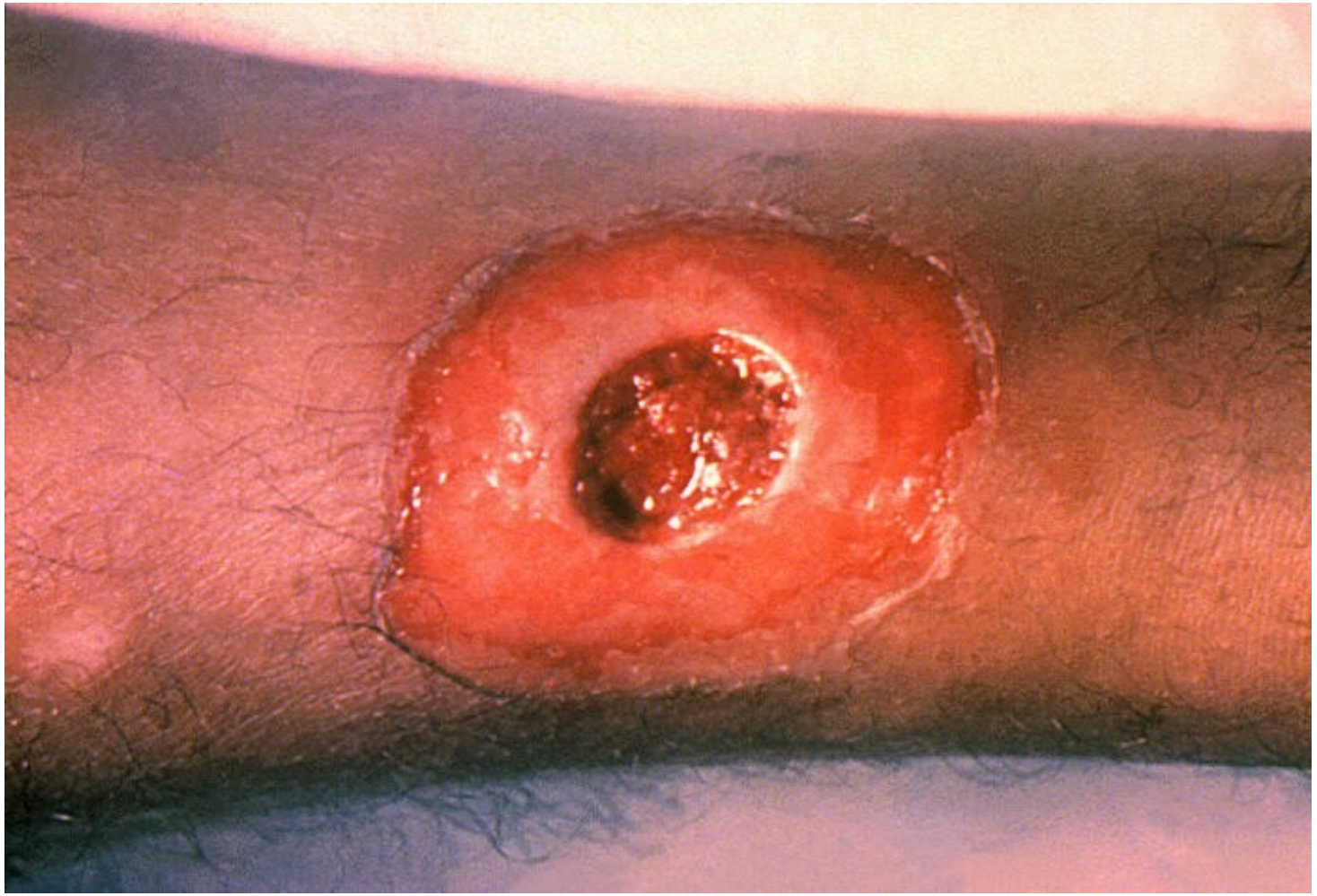
Systemic manifestations

- Systemic toxicity is due to the production and dissemination of the diphtheria toxin
- the heart and nervous tissue are most severely affected
- The risk of developing cardiac and/or neurologic toxicity is proportional to the severity of local infection

Cutaneous Diphtheria

- Indolent, nonprogressive infection characterized by a superficial, ecthymic, nonhealing ulcer with a gray-brown membrane
- Difficult to differentiate from streptococcal or staphylococcal impetigo, and they frequently coexist
- Extremities are more often affected than the trunk or head
- Pain, tenderness, erythema, and exudate

Skin Lesions



Infection at Other Sites

- **occasionally at other sites, such as**
  - **Ear (otitis externa),**
  - **Eye (purulent and ulcerative conjunctivitis), and**
  - **Genital tract (purulent and ulcerative vulvovaginitis)**

DIAGNOSIS

- **Clinical features**
- **Culture- from the nose and throat and any other mucocutaneous lesion**

COMPLICATIONS

- Toxic cardiomyopathy occurs in 10–25% of patients with respiratory diphtheria and is responsible for 50–60% of deaths
- Toxic Neuropathy

  ***Recovery from the myocarditis and neuritis is often slow but usually complete**

TREATMENT

- Antitoxin is the mainstay of therapy
- **Antimicrobial therapy for 14 days** (erythromycin or penicillin) for 14 days
  - Halt toxin production,
  - Treat localized infection, and
  - Prevent transmission of the organism to contacts
- Elimination of the organism should be documented by at least 2 successive negative cultures from the nose and throat (or skin) obtained 24 hr apart after completion of therapy
- Treatment with erythromycin is repeated if either culture yields *C. diphtheriae*

Supportive care

- Patients with pharyngeal diphtheria are placed on droplet precautions, and patients with cutaneous diphtheria are placed on contact precautions
- Cutaneous wounds are cleaned thoroughly with soap and water.
- Bed rest is essential during the acute phase of disease, usually for ≥2 wk until the risk for symptomatic cardiac damage has passed

Prognosis

- Depends on:
  - The virulence of the organism (subspecies *gravis* has the highest fatality),
  - Age,
  - Immunization status,
  - Site of infection, and
  - Speed of administration of the antitoxin.
- The case fatality rate of respiratory tract diphtheria is 10%
- At recovery, administration of diphtheria toxoid is indicated to complete the primary series or booster doses of immunization, because not all patients develop antibodies to diphtheritic toxin after infection.

Modes of control (Prevention)

- Early use of diphtheria antitoxin to neutralize exotoxin
- Penicillin or erythromycin effective for infected patients and asymptomatic carriers
- Active immunization with diphtheria toxoid during childhood (DPT) vaccine
- Antimicrobial prophylaxis for close contacts of patients with diphtheria

Poliomyelitis

- Etiology
  - Polioviruses are non-enveloped, positive-stranded RNA viruses belonging to the Picornaviridae family, in the genus *Enterovirus*, and include three antigenically distinct serotypes (types 1, 2, and 3).
  - Polioviruses spread from the intestinal tract to the central nervous system (CNS), where they cause aseptic meningitis and poliomyelitis, or polio

Epidemiology

- Most devastating result of poliovirus infection is paralysis,
- 90 –95% of infections are inapparent but induce protective immunity
- Clinically apparent but nonparalytic illness occurs in about 5% of all infections
  - paralytic polio occurring in about 1/1,000 infections among infants to about 1/100 infections among adolescents

Transmission

- Humans are the only reservoir
- Spread by the fecal-oral route
- Virus isolated from feces for >2 wk before paralysis to several weeks after the onset of symptoms.

Pathogenesis

- Infect cells by adsorbing to the genetically determined poliovirus receptor
- Penetrates the cell and is uncoated and releases viral RNA
- RNA is translated to produce proteins responsible for replication of the RNA, shut-off of host cell protein synthesis, and synthesis of structural elements that compose the capsid
- Mature virus particles are produced in 6–8 hr and are released into the environment by disruption of the cell

Cont…

- Primarily infects motor neuron cells in the spinal cord (the anterior horn cells) and the medulla oblongata (the cranial nerve nuclei) – this selective attack is characteristic of polio
- Clinical signs of weakness in the limbs develop when more than 50% of motor neurons are destroyed
- In the medulla, less extensive lesions cause paralysis

Pathogenesis cont…

- Entry into mouth
- Replication in pharynx, GI tract, local lymphatics
- Hematologic spread to lymphatics and central nervous system
- Viral spread along nerve fibers
- Destruction of motor neurons

It affects:

- Anterior horn cells
- Cranial nerve motor nuclei
- Reticular formation
- Cerebral motor cortex

It does not affect:

- White matter of the spinal cord
- Cerebral cortex except motor cortex
- cerebellum

- Infants acquire immunity trans placentally from their mothers which disappears at a variable rate during the first 4–6 mo of life
- Active immunity after natural infection is probably lifelong but protects against the infecting serotype only

Clinical Manifestations

- Incubation period is to be 8-12 days, with a range of 5-35 days
- Poliovirus infections may follow one of several courses:
  - Inapparent infection - occurs in 90-95% of cases and causes no disease and no sequelae;
  - Abortive poliomyelitis;
  - Nonparalytic poliomyelitis; or
  - Paralytic poliomyelitis (appears 3-8 days after the initial symptoms)

Outcomes of Poliovirus Infection

Abortive Poliomyelitis

- Nonspecific influenza-like syndrome occurs 1-2 wk after infection (in 5% of patients)
- Fever, malaise, anorexia, and headache, vomiting, abdominal pain, sore throat
- Most recover within 2-3 days
- No neurologic signs or sequelae develop
- Recovery is complete

Nonparalytic Poliomyelitis

- In about 1% of all infected patients
- Usually due to aseptic meningitis
- The above symptoms with more intense headache and vomiting
- Nuchal and spinal rigidity
- In the early stages the reflexes are normally active unless paralysis supervenes
- Changes in reflexes, either increased or decreased, may precede weakness by 12–24 hr
- Lasts for 1-2 days, and progress to paralysis in few
- Most recover

Paralytic Poliomyelitis

- Develops in about 0.1-1 % of persons infected with poliovirus
- Follow nonparalytic or abortive PM

Cont…

- Has three forms

a) Spinal paralytic poliomyelitis - may occur as the 2nd phase of a biphasic illness

  - appear 4 days after symptoms of abortive PM subsided
  - Severe muscle pain is present, and sensory and motor phenomena (e.g., paresthesia, hyperesthesia, fasciculations, and spasms)
  - Asymetric flaccid paralysis
  - The extent of involvement is usually obvious within 2–3 days, usually no progress after 3 days

Spinal cont...

- Paralysis of the lower limbs is often accompanied by bowel and bladder dysfunction
- Little recovery from paralysis is evident with in 6 months
- The return of strength and reflexes is slow and may continue to improve as long as 18 mo after the acute disease
- Lack of improvement from paralysis within the 1st several weeks or months after onset is usually evidence of permanent paralysis
- Usually preceded by muscle pain and ddecreased reflexes
- Cranial nerves,sensation and autonomic NS are spared

b) Bulbar poliomyelitis

- May occur as a clinical entity without apparent involvement of the spinal cord
- Dysfunctions of the cranial nerves and medullary centers
- Rare but life threatening
- Usually cranial nerves IX, X and XII are affected

Bulbar cont...

- Inability to swallow smoothly, resulting in accumulation of saliva in the pharynx
- Irregular respirations that appear interrupted and abnormal
- Absence of effective coughing
- Deviation of the palate, uvula, or tongue
- Involvement of vital centers in the medulla, which manifest as irregularities in rate, depth, and rhythm of respiration; as cardiovascular alterations, including blood pressure changes (especially increased blood pressure), alternate flushing and mottling of the skin, and cardiac arrhythmias; and as rapid changes in body temperature
- Hoarseness, aphonia, and ulti mately asphyxia
- The ***rope sign***, an acute angulation between the chin and larynx caused by weakness of the hyoid muscle

C) **Polio encephalitis**

- Rare form of the disease in which higher centers of the brain are severely involved
- Seizures, coma, and spastic paralysis with increased reflexes
- Irritability, disorientation, drowsiness, and coarse tremors - present with peripheral or cranial nerve paralysis
- Hypoxia and hypercapnia caused by inadequate ventilation due to respiratory insufficiency may produce disorientation without true encephalitis

- **The clinical findings associated with involvement of the respiratory muscles :**
  - anxious expression
  - inability to speak without frequent pauses, resulting in short, jerky, “breathless” sentences
  - increased respiratory rate
  - movement of the ala nasi and of the accessory muscles of respiration
  - inability to cough or sniff with full depth
  - paradoxical abdominal movements
  - relative immobility of the intercostal spaces, which may be segmental, unilateral, or bilateral

Diagnosis

- Consider in any unimmunized or incompletely immunized child with nonspecific febrile illness, aseptic meningitis, or paralytic disease
- Combination of fever, headache, neck and back pain, asymmetric flaccid paralysis without sensory loss, and pleocytosis
- Isolation and identification of poliovirus in the stool, with specific identification of wild-type and vaccine type strains
- Two stool specimens should be collected 24-48 hr apart, as soon as possible after the diagnosis of poliomyelitis is suspected
- CSF – features of viral meningitis with pleocytosis
- Serologic testing demonstrates seroconversion or a fourfold or greater increase in antibody titers, when measured during the acute phase of illness and 3-6 wk later.

Differential Diagnosis

- Guillain-Barré syndrome
- Transverse myelitis
- Traumatic paralysis due to sciatic nerve injury
- Neuropathies

Treatment.

- Usually supportive
- Abortive and non-paralytic PM
  - Supportive treatment with analgesics, sedatives, an attractive diet, and bed rest until the child's temperature is normal
  - Avoidance of exertion for the ensuing 2 wk
  - Careful neurologic and musculoskeletal examinations 2 mo later to detect any minor involvement.

Paralytic PM

- Make the child comfortable
- Maintain adequate fluid and dietary intake
- Minimize skeletal deformity
- Hospitalization with complete physical rest in a calm atmosphere for the first 2-3 weeks
- Moist hot packs may relieve muscle pain and spasm

- Anticipate and treat complications
  - Maintain airway, ensure adequate ventilation – may need tracheostomy
  - Control hypertension, acute gastric dilatation
  - Manage bladder paralysis
  - Hypercalcemia with hypercalciuria and urinary caliculi

Prognosis

- Inapparent, abortive poliomyelitis and aseptic meningitis syndromes - good, death very rare and with no long-term sequelae
- Paralytic PM determined by degree and severity of CNS involvement
- Severe bulbar poliomyelitis – mortality is 60%,
- less severe bulbar involvement and/or spinal poliomyelitis - mortality varies from 5 to 10%

Prognosis cont…

- Maximum paralysis usually occurs 2-3 days after the onset of the paralytic phase of the illness
- The recovery phase lasts about 6 mo, beyond which persisting paralysis is permanent
- Paralysis common in male child and female adults
- Most deaths occur in the first 1-2 weeks
- Major cause of death is respiratory failure

Prevention

- Routine vaccination (EPI)
- Hygiene

Strategy for Polio Eradication

- Strengthen routine EPI for < 1 yr child
- National immunization days
  - Two doses of OPV for all children < 5yrs irrespective of immunization status annually
  - Boost herd immunity and stop wild polio virus spread
- Mopping-up immunization in high risk areas
- AFP surveillance - detect and investigate all cases of AFP in children < 15yrs

Chickenpox

- Primary infection caused by varicella-zoster virus (VZV)
- Results in establishment of a lifelong latent infection of sensory ganglion neurons
- Reactivation of the latent infection causes herpes zoster (shingles**).**

Transmission

- Airborne
- Direct contact
- Transplacental-neonatal chicken pox

- Occurs in epidemics in winter and spring
- Attack rate - home = 65-86%

  School = $\underline{\leq 30\%}$
- Period of infectivity - from 24 to 48 hr before the rash appears and until vesicles are crusted, usually 3–7 days after onset of rash
- incubation period -10–21 day
- Infection confers life long immunity

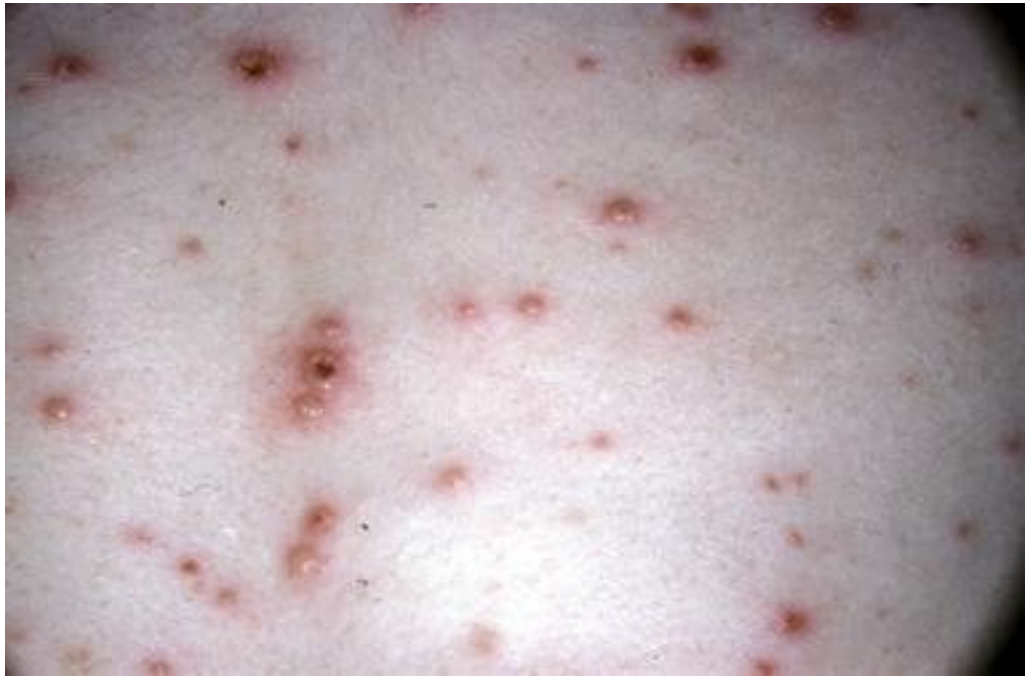
Pathogenesis

- Inoculation of the virus onto the mucosa of the upper respiratory tract and tonsillar lymphoid tissue→ virus replicates in the local lymphoid tissue → subclinical viremia (1 ry viremia) to reticuloendothelial system→ 2nd viremic phase that lasts 3–7 days→ Widespread cutaneous lesions and organ involvement
- Host immune responses limit viral replication and facilitate recovery
- The virus establishes latent infection in the sensory ganglion neurons→ Reactivation→ Herpes zoster

Clinical features

- Develop within 14-16 days after the exposure and typically include a prodrome phase of fever, malaise, or pharyngitis , followed by the development of a generalized vesicular rash, usually within 24 -48 hours
- **Fever and other systemic symptoms persist during the 1st 2–4 days after the onset of the rash**
- The lesions are commonly pruritic and appear as successive crops of vesicles over a three to four day period
- ***Lesions in different stages of development*** on the face, trunk and extremities

- Lesions often appear first on the scalp, face, or trunk
- Starts as macule → papule → vesicle and pustule → crusts
- Pruritic
- Occurs in crops- characteristics
- distribution of the rash is predominantly central or centripetal
- Subclinical varicella is rare; almost all exposed, susceptible persons experience a rash



Complications

- Secondary skin and mucous membrane inf
- Encephalitis, cerebellar ataxia, GBS, Reye syndrome
- Pneumonia, arthritis
- Hepatitis, glomerulonephritis
- Myocarditis, pericarditis,

Treatment

- Supportive
- Isolate the diseased until the rash crusts.
- Keep skin clean by frequent baths or, once the fever has subsided, showers. Cool, wet compresses or tepid water baths help to relieve itching.
- Complications are treated according to symptoms; Secondary bacterial pneumonia is treated with antibiotics.
- Antihistamines may be used to help relieve the itching.
- Acyclovir is used for severe Varicella infections involving the lungs or the brain and in persons with a depressed immune system and in neonates

Prognosis

- Good for healthy children
- Poor for immunocompromized, neonates

Prevention

- Isolation
- Post exposure prophylaxis
  - Vaccine within 3-5 days after exposure
  - Varicella-zoster immune globulin - administered intramuscularly within 96 hr of exposure
- Active immunity
- Newborns whose mothers develop varicella 5 days before to 2 days after delivery should receive 1 vial of VariZIG

Reading Assignment: about

- Mumps
- human papillomavirus
- *Haemophilus influenzae* type B
- Rubella


Thank
You